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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/374,967	08/16/1999	KANWARPAL S. DHUGGA	5718-55	4392

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/02/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/374,967	DHUGGA ET AL.	
	Examiner	Art Unit	
	Mary Schmidt	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,23,24,32,33,41-45,49-59,65-71,73 and 76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,23,24,32,33,41-45,49-59,65-71,73 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Inventors Xun Wang and Benjamin A. Bowen were deleted from the instant Application upon receipt and entry of the Petition (Paper 11) filed October 9, 2001.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-14, 23-24, 32-33, 41-45, 49-59, 65-71, 73 and 76 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the Official Action mailed 07/05/01.

Applicant's arguments filed 10/09/01 have been fully considered but they are not persuasive.

The claims as amended did not change the scope of the claimed compositions. The rejection is maintained on the grounds argued in the previous Official Action.

Applicant argues that the disclosure in the specification is sufficient to teach that Applicant was in possession of the scope of the claimed constructs at the time the invention was made. Specifically, Applicant argues that the specification taught specific sequences to the maize GDP-mannose pyrophosphorylase, mechanics for hybridization to such sequences, and that such disclosure reasonable conveys to the artisan that the inventor had possession at the time the

invention was made of sequences which would hybridize to the specifically disclosed sequences. Applicant further cites MPEP 2164.08(b) as teaching that inoperative embodiments within the scope of the claim does not necessarily render a claim nonenabled for that scope. This citation was made in response to the argument that any sequence having 20 nucleotide homology to the disclosed SEQ ID NOS. would not have an expectation of providing a GDP-mannose pyrophosphorylase having the function of such a protein. Applicant thus argues that Applicant was in possession of the scope of the instantly claimed invention at the time the invention was made.

In response, although the specification does teach specific maize GDP-mannose pyrophosphorylase, as well as conditions for hybridization of nucleic acid sequences to the disclosed GDP-mannose pyrophosphorylase sequences, such a disclosure does not reasonably convey to the skilled artisan that Applicant was in possession of the scope of the claimed sequences. As argued previously, despite the ability to hybridize sequences to a known sequence, even for the purpose of identifying sequences with high homology to said sequences, the mere identification of such a sequence does not render the skilled artisan with a nucleic acid sequence which could be considered a GDP-mannose pyrophosphorylase. For instance, as argued previously, any sequence having a 20 base region of homology to the disclosed sequences does not have the expectation that such a sequence would be considered a GDP-mannose pyrophosphorylase by function. Applicant argues that MPEP 2164.08(b) doesn't require all claimed embodiments to be operative. However, whether the claimed sequences are operative or

not does not render the claimed sequences adequately described. The nucleic acid sequences may be operative, but not considered a maize GDP-mannose pyrophosphorylase. Furthermore, the MPEP states that the standard is "whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art." The references cited in the scope of enablement rejection teach the unpredictability in the art for determination of protein structure/function from knowing a nucleic acid sequences. Even in cases of families of high homology, there are deviant proteins which do not function in a manner similar to the other family members. Thus each protein must be considered on an individual basis. The specification as filed teaches some GDP-mannose pyrophosphorylase sequences, as well as hybridization conditions for detection of nucleic acids which would hybridize the disclosed nucleic acid sequences, does not provide sufficient guidance to determine which of such sequences would be considered a GDP-mannose pyrophosphorylase. Thus, the specification as filed does not teach that Applicant was in possession of any plant GDP-mannose pyrophosphorylase; sequences having 20 contiguous nucleotides of SEQ ID NO:1; sequences having 90% homology to any plant GDP-mannose pyrophosphorylase, SEQ ID NO:2, SEQ ID NO:1 or any 20 contiguous nucleotides of SEQ ID NO:1; any sequence that hybridizes to any of those sequences, or any antisense, fragment or variant of any of such sequences.

4. Claims 1-14, 23-24, 32-33, 41-45, 49-59, 65-71, 73 and 76 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOS:1 and 2, expression cassettes comprising said sequences, plant cells and transgenic plants comprising said sequences, methods of expressing said sequences or antisense to said sequences in a plant cell or plant, does not reasonably provide enablement for the scope of possible nucleic acid sequences or protein sequences claimed nor use thereof in plant cells or plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons of record as set forth in the Official Action mailed 07/05/01.

Applicant's arguments filed 10/09/01 have been fully considered but they are not persuasive.

The claims as amended did not change the scope of the claimed compositions. The rejection is maintained on the grounds argued in the previous Official Action.

Applicant requests on page 11 of the response that "examiner make explicit which claims the statement refers to. Variants and/or amino acid substitutions of the coding region are not claimed in the present invention."

In response, the assertion that there is "little guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change..." made in the previous Action, is in response to the breadth of claim 1 for instance. Claim 1, step (g), which states "a

nucleotide sequence encoding an antisense RNA of a nucleotide sequence of a), b), c), d), e) or f); and fragments and *variants* thereof." Claim 1 thus discusses variants of a coding region as written. The statement was also in regards to the breadth of the nucleic acid sequences claimed in sections a) through f) of claim 1. Specifically, the asserted utility of the claimed sequences in the specification as filed is the role of the disclosed sequences, maize GDP-mannose pyrophosphorylases as proteins involved in gum production (see page 4, last para., of the specification for instance). The disclosure of the specification does not support or enable the skilled artisan for using other types of proteins. The claims as written broadly read on sequences which comprise variants, fragments, and other sequences which hybridize to the disclosed sequences. However, sufficient guidance is not supplied in the specification to teach one skilled in the art how to make other nucleic acid sequences, even by hybridization, which would be considered to make a maize GDP-mannose pyrophosphorylase having the disclosed utility. As such, one skilled in the art would necessarily practice "trial and error" experimentation beyond the disclosure to take any such sequence having the capacity to hybridize to the disclosed sequences and generating a functional maize GDP-mannose pyrophosphorylase as enabled in the instant disclosure.

With regard to the question about where the specification teaches screening for active muteins, this instant specification does not specifically use the word "muteins." For clarification, the intended point of this assertion in the prior Action was that the specification teaches particular sequences (SEQ ID NO:1 as the nucleic acid which encodes the protein in SEQ ID NO:2) and not

variants of such sequences. For instance, the broadly claimed sequences read on any sequence which hybridizes to SEQ ID NO:1, thus encompassing variants of it, and variants of the disclosed protein in SEQ ID NO:2. Such variants encompass sequences having different regions from the specifically disclosed sequences such as muteins. It is argued that such sequences as broadly claimed are not enabled by the instant disclosure. Although the specification teaches methods of hybridizing to SEQ ID NO:1 for instance to determine other potential GDP-mannose pyrophosphorylases and references to teach how to align such sequences to known sequences in the art to determine the homology of the identified sequences (see page 12 of the specification for instance), the ability to find homologous regions in a new protein to known proteins does not enable one skilled in the art to use such as protein for the reasons argued previously.

Applicant argues on page 13 of the response that a majority of the sequences claimed in claim 1 would be functional. As argued in the prior Action and above, the claims read on a broad scope of sequences which hybridize to the disclosed, sequences, or are just generally considered plant GDP-mannose pyrophosyphorylases. The claims read on sequences having more breadth than those which have 90% homology to SEQ ID NO:1. Applicant points to an amino acid sequence homology comparison between GDP-mannose pyrophosyphorylases from different organisms showing regions of significant homology between the GDP-mannose pyrophosphorylases. At the time the invention was made however, not all of the disclosed sequences argued in the response were available and thus one skilled in the art would not have known at the time the invention was made that a certain scope of GDP-mannose

pyrophosphorylases had certain regions of high homology. Additionally, there is a high level of unpredictability that any sequence which has a 20 base pair contiguous region of SEQ ID NO:1 or any antisense, fragments or variants as broadly claimed would function as a GDP-mannose phosphorylase, or to inhibit such a gene as broadly claimed. To design a functional antisense, the exact target sequence must be known. Furthermore, specific regions of the target sequence must be known to be capable of binding an antisense oligonucleotide since not all regions of the gene are accessible to antisense binding due to stearic hindrance. For the reasons summarized above and stated in the previous Official Action, the claims as written lack enablement to make and use the scope of the claimed sequences.

Due to the lack of guidance in the specification or the art for making and using the scope of the claimed sequences, one skilled in the art would necessarily practice an undue amount of experimentation to make and use the invention as claimed.

5. Claims 56-59 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the Official Action mailed 07/05/01.

Applicant's arguments filed 10/09/01 have been fully considered but they are not persuasive.

Applicant first argues that the DeLuca reference "offers no less than eleven examples of success in altering metabolic pathways in plants via transformation with exogenous genes... page 225N, paragraph 5; page 226N, paragraph 2; page 227N, paragraphs 2, 3, 4, 5, 7 and 10; and page 228N, paragraphs 2, 3, and 4."

Paragraph 5 on page 225N discusses changing flower color in plants. The cited paragraphs on pages 226N, 227N and 228N teach examples in the art for different types of changes in enzyme concentration. However, none of the cited examples are considered to provide a direct nexus to one skilled in the art as to how to use the scope of claimed sequences for any gum manipulation (both increasing and decreasing) as broadly claimed. DeLuca is relied on primarily to teach the "numerous empirical *attempts*", not successes, "to redirect metabolic pathways." They teach specifically that "in some cases spectacular results are obtained, whereas on many occasions desired goals have been impossible to achieve. Several reasons could be invoked for a particular failure... but most of the answers will involve detailed analyses of the targeted biochemical pathways and their transgenic counterparts. The results from these types of experiments should serve to develop more rational approaches to metabolic engineering of plants." (P. 228N) Thus, while Applicant is correct that several examples are taught by DeLuca for success in different types of metabolic engineering, none of these examples is considered to correlate to the claimed metabolic pathway changes, and DeLuca clearly states that on "many occasions" results are not predictable.

Stephanopoulous et al. is further relied upon to teach on page 395, col. A, that "in summary there are three outstanding challenges in metabolic engineering from a network analysis point of view: (1) locating the critical branch points in the bioreaction network; (2) selecting the most appropriate type of genetic modification; (3) identifying the location(s) of metabolic control as target(s) of further manipulation." Neither the specification nor the art has provided guidance as to these unpredictable factors in design of methods for gum manipulation as broadly claimed. Note that U.S. Patent 6,363,669, exemplifies different ratios of xanthan gum weights as well as other types of gums such as guar gum, tamarind gum and bean gum. Neither the specification nor the art taught one skilled in the art at the time the invention was made how to correlate any manipulation of the claimed sequences for downsteam manipulation of any gum production as broadly claimed. Specifically, there was no guidance for the unpredictable factors cited by Stephanopoulous et al. for the instantly claimed metabolic pathways prior to the time the invention was made. In the absence of such teaching, one skilled in the art would have necessarily practiced "trial and error" experimentation to practice the claimed invention.

Finally, although Ritter et al. taught the role of GDP-mannose generically in the production of sugars to form oligosaccharides, such a disclosure does not overcome the unpredictability in the art of engineering specific plant metabolic pathways taught by DeLuca and Stephanopoulous et al. above. As such, one skilled in the art would necessarily practice undue experimentation to make and use the invention as broadly claimed.

6. The claims remain free of the prior art since the art does not teach sequences of plant GDP-mannose pyrophosphorylase as claimed prior to the filing of the instant invention.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

M. M. Schmidt
December 31, 2001